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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,428	05/10/2005	Jeffrey Keller Teumer	50393/004001	5032

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EXAMINER	
GOUGH, TIFFANY MAUREEN	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 08/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/534,428	TEUMER ET AL.	
	Examiner	Art Unit	
	Tiffany M. Gough	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21 and 29-50* is/are pending in the application.

4a) Of the above claim(s) *34-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21 and 29-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/10/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of claims 1-21,29-33 in the reply filed on 07/24/2006 is acknowledged.

Claims 34-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16,29-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 16,30 and 31 fail to distinctly claim applicant's invention because "a serum-free component" of the conditioned medium is claimed. It is unclear if this "component" is separate from the medium.

Claim 29 does not particularly point out the subject matter regarded as applicant's invention because applicant claims an "established" cell line. It is unclear what an "established" cell line is in regards to applicant's invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,7-10,13,17,19 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 99/01034.

Applicant claims a method for cultivating hair inductive cells. The method comprises the steps of culturing the hair inductive cells, dermal papilla cells, in a non-epidermal tissue derived cell conditioned culture medium in which the hair inductive potential of the hair inductive cells is maintained. The medium is to consist essentially of the conditioned medium ,is free of recombinant genes or products thereof and is concentrated. The method further comprises the step of harvesting or isolating cultured or subcultured hair inductive cells.

WO 99/01034 discloses a method for producing new hair growth comprising culturing human dermal papilla cells in a medium conditioned with human keratinocytes. They show that co-cultivation allows rat papilla cells to retain their hair inducing capabilities through 56 passages (p.2, lines 7-10). WO'034 disclose that the human papilla cells cultured in a keratinocyte conditioned medium can expand rapidly for many passages in vitro while maintaining their hair inducing properties (p.2,lines 27-29). The keratinocytes are preferably taken from the outer root sheath of the hair follicle where

the epithelial stem cells are thought to reside, i.e non-epidermal. The keratinocytes may be autologous or allogenic in source (p.4, lines 10-22). After culturing the papilla cells in the keratinocyte conditioned media, the papilla cells are then harvested and can be used directly or centrifuged, i.e. concentrated (p.5, lines 1-4). The culture medium does not contain any recombinant genes or products thereof.

The reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-15,17,19-21,29 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/01034 and WO 00/69449 in view of Keller et al (Frontiers in

Bioscience, 1996), Hibberts et al (Journal of Endocrinolgy, 1998) and Van Nispen (US 5,002,881, 1991).

Applicant claims a method for cultivating hair inductive cells. The method comprises the steps of culturing the hair inductive cells, dermal papilla cells, in a non-epidermal tissue (non-ectodermal) of mesodermal or endodermal origin derived cell conditioned culture medium in which the hair inductive potential of the hair inductive cells is maintained. The conditioned cells are prostate epithelial cells or human dermal fibroblasts or may also be obtained using a cell line, which is derived from a donor who has been screened and tested for risk factors associated with transplantation.The hair inductive cells are allogeneic or autologous to the non-epidermal tissue. The medium is to consist essentially of the conditioned medium, is free of recombinant genes or products thereof, viral vectors and is concentrated by ultrafiltraion. The medium is preferably frozen prior to use. The method further comprises the step of harvesting or isolating cultured or subcultured hair inductive cells.

WO 99/01034 discloses a method for producing new hair growth comprising culturing human dermal papilla cells in a medium conditioned with human keratinocytes. They show that co-cultivation allows rat papilla cells to retain their hair inducing capabilities through 56 passages (p.2, lines 7-10). WO'034 disclose that the human papilla cells cultured in a keratinocyte conditioned medium can expand rapidly for many passages in vitro while maintaining their hair inducing properties (p.2,lines 27-29). The keratinocytes are preferably taken from the outer root sheath of the hair follicle where

the epithelial stem cells are thought to reside, i.e non-epidermal. The keratinocytes may be autologous or allogenic in source (p.4, lines 10-22). After culturing the papilla cells in the keratinocyte conditioned media, the papilla cells are then harvested and can be used directly or centrifuged, i.e. concentrated (p.5, lines 1-4).

WO 00/69449 disclose conditioned cell culture medium compositions and their methods of use. The medium may be conditioned with **any eukaryotic cell type** (p.5,lines 30-34) including human hair papilla cells (p.45,lines 34),epithelial cells, stromal, parenchymal, mesenchymal cells, liver reserve cells, neural stem cells, pancreatic stem cells, fibroblasts including human dermal fibroblasts, endothelial cells, pericytes, macrophages, monocytes, plasma cells, mast cells, adipocytes, chondrocytes, keratinocytes (p.5,lines 32-35,p.8,lines 8-12,p.9 lines 31-35) from corresponding tissues including bone marrow, skin, liver, pancreas, kidney as well as **genitourinary tract**, i.e. encompassing the prostate (p.12,lines 13-20). Cell lines may also be used in the conditioned medium but are carefully screened for human and animal pathogens, i.e tested for risk factors associated with transplantation (see p.14,lines 6-10). The medium may contain, but does not require the addition of additional growth factors and proteins, i.e, consisting essentially of the conditioned medium (p.13, lines 8-12) and is serum-free (p.11, lines 4-7). The medium may be in any form such as liquid, frozen, lypholized, or dried (p.6,lines 18-20). The compositions are used to culture cells and further is formulated for methods of stimulating hair growth

(p.7, lines 18-31). The conditioned medium is also concentrated by any methods known in the art (p.29,lines 1-9, p.46 lines 2-3).

Neither reference teaches cultivating hair inductive cells such as dermal papilla or sheath cells in conditioned medium conditioned with prostate epithelial cells.

However, WO 00/69449 strongly suggests a culture media used for cultivation of cells used in a method for stimulating hair growth, particularly they disclose a media conditioned with cells from the genitourinary tract, i.e. prostate epithelial cells, which is formulated to culture cells used in methods of stimulating hair growth. Given what is known in the art of the importance of dermal papilla cells in the development of hair, it would be obvious to one of ordinary skill in the art at the time of the invention to cultivate dermal papilla cells in a conditioned medium formulated for stimulating hair growth.

Further, It is known in the art that the development of the hair follicle depends on a mesenchymal-epithelial interaction, i.e dermal papilla-keratinocytes. The same is true for prostate tissue, i.e. prostate stroma-prostate epithelial cells, as is disclosed by Keller et al (Frontiers in Bioscience, 1996). It is also known that androgen plays a role in the development of both. For example, activated andogen receptors suppress the growth of follicle populations in those exhibiting male pattern baldness and altered androgen receptors have been linked to recurrence of prostate cancer (Keller, p.2). Further, as is known in the art, the development of hair follicles is intimately associated with dermal

papilla cells as is androgen through androgen receptors, which are known to effect hair follicle proliferation by modulating dermal papilla activity through growth factors. Androgen also modulates expression of growth factors in the prostate stroma (mesoderm) (p.7).

Hibberts et al (Journal of Endocrinolgy, 1998) disclose that androgens are the most obvious regulators of normal hair growth and are a prerequisite for male pattern baldness. As is known in the art, the hair follicle is composed mainly of epithelial cells which protrudes down to the epidermis and dermis of the skin, enveloping at the base the mesenchyme-derived dermal papilla cells. Androgens act on the hair follicle via the mesencyme-derived dermal papilla, altering the production of mitogenic factors and extracellular matrix factors, which influence the epithelial cells.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have cultivated hair inductive cells such as dermal papilla cells in a medium conditioned with prostate epithelial cells because it is known in the art that both hair follicles and the prostate develop via mesenchymal-epithelial interactions, i.e dermal papilla-keratinocytes and prostate stroma-prostate epithelial cells and both hair follicle and prostate development are androgen modulated, plus there has been an observed association between men with male pattern baldness and benign prostate hyperplasia (see Oh et al, Urology, vol 51 1998), therefore, one would expect to

establish the required mesenchymal-epithelial interaction between dermal papilla cells and prostate epithelial cells required for hair follicle development.

One of ordinary skill in the art would have been motivated to condition a hair inductive cell medium with prostate epithelial cells to achieve a mesenchymal-epithelial interaction necessary for the development of hair follicles given that both prostate and hair cell development depend on this interaction and are androgen mediated. Thus, one would have expected success in cultivating hair inductive cells in the presence of this specific epithelial cell.

Neither reference teach concentrating the medium by ultrafiltration, however, ultrafiltration is known in the art as a concentration method used in concentrating mediums, as evidenced by US 5,002,881, which teaches using ultrafiltration to concentrate a medium (see col.3 lines 30-40).

Claims 1,18 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/01034.

Applicant claims a method for cultivating hair inductive cells. The method comprises the steps of culturing the hair inductive cells in a non-epidermal tissue derived cell conditioned culture medium. The hair inductive cells are subcultured in the medium for 7 passages or more.

WO 99/01034 discloses a method for producing new hair growth comprising culturing human dermal papilla cells in a medium conditioned with human keratinocytes. They show that co-cultivation allows rat papilla cells to retain their hair inducing capabilities through 56 passages (p.2, lines 7-10). WO'034 disclose that the human papilla cells cultured in a keratinocyte conditioned medium can expand rapidly for many passages in vitro while maintaining their hair inducing properties (p.2,lines 27-29). The keratinocytes are preferably taken from the outer root sheath of the hair follicle where the epithelial stem cells are thought to reside, i.e non-epidermal. The keratinocytes may be autologous or allogenic in source (p.4, lines 10-22). After culturing the papilla cells in the keratinocyte conditioned media, the papilla cells are then harvested and can be used directly or centrifuged, i.e. concentrated (p.5, lines 1-4).

Although, WO'034 does not specifically teach the number of passages of the dermal papilla cells, they do teach that the cells can expand for many passages and further teach the ability of rat cells under the same conditions to retain their hair inducing properties through 56 passages.

Thus, it would be obvious to one of ordinary skill in the art at the time the invention was made to cultivate dermal papilla cells in a conditioned medium with cells of non-epidermal origin and expect success in maintaining the hair inducing properties through passages of more than seven.

One of ordinary skill in the art would have been motivated to cultivate dermal papilla cells in a medium conditioned with cells of non-epidermal origin with the goal of maintaining the papilla cells hair inducing properties for more than seven passages

given that WO'034 discloses co-cultivation allows rat papilla cells to retain their hair inducing properties through 56 passages and that human papilla cells cultured under the same conditions are can expand and maintain this property for many passages.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tiffany M. Gough whose telephone number is 571-272-0697. The examiner can normally be reached on M-F 8-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

tmg

RUTH DAVIS
PRIMARY EXAMINER